

**Remarks**

Claims 1 - 14 are pending in the present application. The following rejections are at issue and are set forth by number in the order in which they are addressed:

1. Claims 3 and 6 are rejected under 35 U.S.C. §112, second paragraph as indefinite;
2. Claims 1 - 4, 6 and 12 - 14 are rejected under 35 U.S.C. §102(b) as being anticipated by Allen-Hoffmann et al. (U.S. Pat. No. 5,989,837);
3. Claims 1 - 2, 4 - 9 and 12 - 13 are rejected under 35 U.S.C. §102(b) as being anticipated by Yang et al. (2000);
4. Claims 1 - 2 and 4 - 13 are rejected under 35 U.S.C. §103(a) as unpatentable over Yang et al. (2000);
5. Claims 1 - 4 and 6 - 14 are rejected under 35 U.S.C. §103(a) as unpatentable over Allen-Hoffmann et al. (U.S. Pat. No. 5,989,837); and
6. Claims 1 - 14 are rejected under 35 U.S.C. §103(a) as unpatentable over Yang et al. in view of Allen-Hoffmann et al. (U.S. Pat. No. 5,989,837).

Claims 1, 3, and 6 have been amended. Unless otherwise noted, the claims have been cancelled or amended to further Applicant's business interests and the prosecution of the present application in a manner consistent with the PTO's Patent Business Goals (PBG; 65 Fed. Reg. 54603 (September 8, 2000), and not in acquiescence to the Examiner's arguments and while reserving the right to prosecute the original (or similar) claims in the future. None of the claim amendments made herein are intended to narrow the scope of any of the amended claims within the meaning of *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 234 F.3d 558, 56 USPQ2d 1865 (Fed. Cir. 2000) or related cases. The amendments find more than ample support in the specification and the claims as originally filed. See, for example, page 39, lines 19 - 31.

**1. The Claims are Definite**

Claims 3 and 6 are rejected under 35 U.S.C. §112, second paragraph as indefinite. Claims 11-13, 17, 68, 29-33, and 60-64 have been cancelled. Claims 3 and 6 have been amended to spell out the acronyms NIKS and NHDF. These claims have been amended to further

Applicant's business interests and the prosecution of the present application in a manner consistent with the PTO's Patent Business Goals (PBG; 65 Fed. Reg. 54603 (September 8, 2000)), and not in acquiescence to the Examiner's arguments and while reserving the right to prosecute the original (or similar) claims in the future. None of the claim amendments made herein are intended to narrow the scope of any of the amended claims within the meaning of *Festo Corp. v. Shokestu Kinzoku Kogyo Kabushiki Co.*, 234 F.3d 558, 56 USPQ2d 1865 (Fed. Cir. 2000) or related cases. Thus, the scope of the claims has not changed due to these amendments.

**2. The Claims are not Anticipated by Allen-Hoffmann et al.**

Claims 1 - 4, 6 and 12 - 14 are rejected under 35 U.S.C. §102(b) as being anticipated by Allen-Hoffmann et al. (U.S. Pat. No. 5,989,837). The Federal Circuit has stated the relevant analysis for anticipation as follows:

A claim is anticipated only if each and every element as set forth in the claims is found, either expressly or inherently described, in a single prior art reference."

*Verdegaal Bros. v. Union Oil Co. Of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Applicants respectfully note that the organotypic culture procedure is described in detail by Allen-Hoffmann et al. at column 18, line 54 - column 19, line 8. In particular, Allen-Hoffmann et al. states that "Cells were allowed to attach 2 hours before adding an additional 13 mls of media (Day 0). On days 1 and 2 cells were refed. On Day 4, cells were lifted to the air interface with cotton pads and switched to cornification medium . . . ." Thus, the seeded dermal equivalent is resubmerged in medium for a substantial period of time. This is contrast to the amended claims, which require culture of the seeded dermal equivalent at the air interface until stratification occurs. As a result, Allen-Hoffmann et al. does not teach each element of the pending claims. Accordingly, Applicants respectfully submit that this ground of rejection be removed and the claims passed to allowance.

**3. The Claims are not Anticipated by Yang et al.**

Claims 1 - 2, 4 - 9 and 12 - 13 are rejected under 35 U.S.C. §102(b) as being anticipated by Yang et al. (2000). On page 10, Yang et al. states that:

After the culture of dermal equivalent for 7 days, the culture medium was aspirated to leave the gel surface exposed, and epidermal keratinocytes were applied to the surface at

an initial density of  $1 \times 10^5$  cells/cm<sup>2</sup>. The construct was submerged under keratinocyte culture medium inside and outside the of the culture insert to allow these keratinocytes to spread and cover the surface of the dermal equivalent, which is accomplished in approximately seven days of incubation.

Thus, the seeded dermal equivalent is resubmerged in medium for a substantial period of time. In view of this teaching, Applicants respectfully submit that the Examiner's assertion at page 5 of the Office Action that the dermis "is further cultured at the air-liquid interface (p.10, production of artificial skin)" is incorrect. The construct is only cultured at the air interface after seven days of submersion. This is in contrast to the amended claims, which require culturing the seeded dermal equivalent at the air interface until stratification occurs. As a result, Yang et al. does not teach each element of the pending claims. Furthermore, Applicants note that Yang et al. does not teach the incubation time elements of Claims 8 and 9. Accordingly, Applicants respectfully submit that this ground of rejection be removed and the claims passed to allowance.

**4. The Claims are not Obvious over Yang et al.**

Claims 1 - 2 and 4 - 13 are rejected under 35 U.S.C. §103(a) as unpatentable over Yang et al. (2000). A *prima facie* case of obviousness requires the Examiner to provide a reference(s) which (a) discloses all of the elements of the claimed invention, (b) suggests or motivates one skilled in the art to combine the claimed elements to produce the claimed combination, and (c) provides a reasonable expectation of success should the claimed combination be carried out. Failure to establish any one of these three requirements precludes a finding of a *prima facie* case of obviousness and without more entitles the Applicants to allowance of the claims in issue. See, e.g., *Northern Telecom Inc. v. Datapoint Corp.*, 15 USPQ2d 1321, 1323 (Fed. Cir. 1990). Applicants respectfully submit that the cited reference neither teaches nor suggests each element of the claims and that the cited reference has been improperly modified by the Examiner.

In particular, as described above, Yang et al. teaches submerging the seeded dermal equivalent in medium for a substantial period of time following seeding. In view of this teaching, Applicants respectfully submit that the Examiner's assertion at page 6 of the Office Action that the dermis "is further cultured at the air-liquid interface (p.10, production of artificial skin)" is incorrect. The construct is only cultured at the air interface after seven days of submersion. This is in contrast to the amended claims, which require culturing the seeded

dermal equivalent at the air interface until stratification occurs. As a result, Yang et al. does not teach each element of the pending claims. Accordingly, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness with respect to the rejected claims. As such the claims should be passed to allowance.

With respect to Claims 7 -11, Applicants further note that the Examiner admits at page 6 of the Office Action that "Yang does not teach the method wherein the incubating lasts for about 24 hours, or 6 - 24 hours." The Examiner then states that:

However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize incubation times as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the incubation times of Yang with a reasonable expectation for successfully making a stratified skin equivalent.

Applicants respectfully submit that this conclusory statement falls far short of the standards established by the Federal Circuit for providing a motivation to combine or modify references. The Examiner has provided no objective evidence, other than this conclusory statement, that supports the proposition that one of skill in the art would modify the teaching of Yang et al. by adding the step of preincubation of the dermal equivalent at the air interface. Indeed, the Examiner cannot establish as *prima facie* case of obviousness by simply listing the elements from the claims and then stating that they are "well-known" or "common features." The Federal Circuit has specifically discredited this approach. Specifically, the Federal Circuit has held that:

The factual inquiry whether to combine references must be thorough and searching. It must be based on **objective evidence** of record. **This precedent has been reinforced in myriad decisions, and cannot be dispensed with.**

*See, In re Lee*, 277 F.3d 1338, 1344 (Fed. Cir. 2002); internal citations omitted; emphasis added. Furthermore, an Examiner may not simply rely on conclusory statements even for what they think might be common sense or well known in the art:

The 'common knowledge and common sense' on which the Board relied in rejecting Lee's application are not the specialized knowledge and expertise contemplated by the Administrative Procedure Act. **Conclusory statements such as those here provided do not fulfill the agency's obligation.** This court explained in *Zurko*, 258 F.3d at 1385, 59 USPQ2d at 1697 that 'deficiencies of the cited references cannot be remedied by the Board's general conclusions about what is 'basic knowledge' or 'common sense.' The Board's findings must extend to all material facts and must be documented on record, lest the 'haze of so-called expertise' acquire insulation from accountability. 'Common

knowledge and common sense,' even if assumed to derive from the agency's expertise, do not substitute for authority when the law requires authority.

*Id.* at 1344-1345 (emphasis added).

Thus, according to recent Federal Circuit precedent, an Examiner cannot rely on what is "well known or routine in the art", as is the case with the instant rejection, to modify or combine references. The Applicants respectfully submit that the Examiner's conclusory statement as to what is "well known or routine in the art" is an insufficient replacement for what is required by the law - authority for the position asserted by the examiner.

Indeed, the Examiner appears to have relied on hindsight reconstruction to make these rejections. The modifications (i.e., what is "well known or routine in the art") are only well known or routine in the art when viewed in light of Applicant's specification. Such hindsight reconstruction is also inconsistent with current Federal Circuit precedent. The Examiner has not shown reasons **why** a skilled artisan would make the modification. Such unsupported statements are inconsistent with current Federal Circuit precedent:

The Board did not . . . explain what specific understanding or technological principal within the knowledge of one of ordinary skill in the art would have suggested the combination. Instead, the Board merely invoked the high level of skill in the art. If such a rote invocation could suffice to supply a motivation to combine, the more sophisticated scientific fields would rarely, if ever, experience a patentable technological advance. Instead, in complex scientific fields, the Board could routinely identify the prior art elements in an application, invoke the lofty level of skill, and rest its case for rejection. To counter this potential weakness in the obviousness construct, the suggestion to combine requirement stands as a critical safeguard against hindsight analysis and rote application of the legal test for obviousness.

*In re Rouffet et al.*, 149 F.3d 1350, 47 USPQ2d 1453 at 1458 (Fed. Cir. 1998). By simply reciting a list of elements and stating that such elements are "well known or routine in the art", the Examiner is apparently relying on the high level of skill in the art to guide the modification. Applicants can find no other reasoning supporting the modification. The Examiner's apparent reliance on the high level of skill in the art is expressly forbidden by the Federal Circuit.

For the foregoing reasons, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness with respect to the rejected claims. As such the claims should be passed to allowance.

**5. The Claims are not Obvious over Allen-Hoffmann et al.**

Claims 1 - 4 and 6 - 14 are rejected under 35 U.S.C. §103(a) as unpatentable over Allen-Hoffmann et al. (U.S. Pat. No. 5,989,837). The standards for making a *prima facie* case of obviousness are discussed above. As above, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness because the cited reference does not teach each element of the claims.

As above, Applicants respectfully note that the organotypic culture procedure is described in detail by Allen-Hoffmann et al. at column 18, line 54 - column 19, line 8. In particular, Allen-Hoffmann et al. states that "Cells were allowed to attach 2 hours before adding and additional 13 mls of media (Day 0). On days 1 and 2 cells were refed. On Day 4, cells were lifted to the air interface with cotton pads and switched to cornification medium . . . ." Thus, the seeded dermal equivalent is resubmerged in medium for a substantial period of time. This is contrast to the amended claims, which require culture of the seeded dermal equivalent at the air interface until stratification occurs. As a result, Allen-Hoffmann et al. does not teach each element of the pending claims. Accordingly, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness with respect to the rejected claims. As such the claims should be passed to allowance.

Moreover, Applicants again respectfully submit that with respect to Claims 7 - 11 the Examiner has provided no objective evidence as to why a person of ordinary skill in the art would be motivated to modify the cited reference. Applicants note that the Examiner admits on page 8 of the Office Action that "Allen-Hoffmann does not teach the methods with the claimed incubation times." The Examiner then provides the following the conclusory motivation statement:

However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize incubation times as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the incubation times of Allen-Hoffmann with a reasonable expectation for successfully making a stratified skin equivalent.

As discussed in detail above, the Federal Circuit requires that the Examiner come forth with objective evidence of why references should be modified or combined. Moreover, the Examiner cannot rely on what is supposedly well known or routine within the art as a substitute for the required evidence. In the instant rejection, the Examiner relies completely on the high level of skill in the art to establish the motivation to modify the cited reference. The Examiner's apparent reliance on the high level of skill in the art is expressly forbidden by the Federal Circuit.

For the foregoing reasons, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness with respect to the rejected claims. As such the claims should be passed to allowance.

**6. The Claims are not Obvious Over Yang et al. in view of Allen-Hoffman et al.**

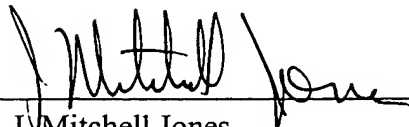
Claims 1 - 14 are rejected under 35 U.S.C. §103(a) as unpatentable over Yang et al. in view of Allen-Hoffmann et al. (U.S. Pat. No. 5,989,837). As can be seen from the discussion above, the cited references, either alone or in combination, fail to teach each element of amended claims, which require culture of the seeded dermal equivalent at the air interface until stratification occurs. Moreover, as discussed above, the Examiner cannot rely on what is supposedly well known or routine within the art as a substitute for the required evidence of why the references should be combined or modified. In the instant rejection, the Examiner relies completely on the high level of skill in the art to establish the motivation to modify the cited reference. The Examiner's apparent reliance on the high level of skill in the art is expressly forbidden by the Federal Circuit. Accordingly, Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness with respect to the rejected claims. As such the claims should be passed to allowance.

**C O N C L U S I O N**

All grounds of rejection and objection of the Office Action of July 29, 2003 having been addressed, reconsideration of the application is respectfully requested. It is respectfully submitted that the invention as claimed fully meets all requirements and that the claims are worthy of allowance. Should the Examiner believe that a telephone interview would aid in the

prosecution of this application, Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

Dated: October 28, 2003

  
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